REMARKS

Applicants have amended the Specification. The amendments do not entail the introduction of new matter. Specifically, Applicants have inserted the U.S. Government support statement, and deleted a paragraph on page 24 that is identical to the immediately preceding paragraph.

In the Office Action, the Examiner indicates that Claims 1-17 are at issue in the present Application. However, Applicants note that Claims 14-17 were cancelled in the Preliminary Amendment dated February 11, 1998, and submitted with the present Continuation Application when filed.

The Examiner has rejected Claims 1-13 under 35 U.S.C. §112, first paragraph, as allegedly failing to provide an enabling disclosure for specific threonine-kinase inhibitors. The Examiner has also rejected Claims 14-17 under 35 U.S.C. §101, as claiming the same invention as that of Claims 1-4 of U.S. Patent No. 5,798,380. However, Applicants note that Claims 1-4 were cancelled at the time that the present Continuation Application was filed. Thus, Applicants believe that this rejection is moot, and it is not further addressed herein. Finally, Claims 1-13 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting, as being allegedly unpatentable over Claims 1-4 of U.S. Patent No. 5,798,380. Applicants appreciatively note that the Examiner has removed the other rejections (*e.g.*, rejections under 35 U.S.C. §§102 and 103).

Applicants believe that the following remarks traverse the Examiner's rejection of the claims.

(1) Claims 1-13 are Enabled, and Patentable Under 35 U.S.C. §112, First Paragraph

In the Office Action, the Examiner rejected Claims 1-13 under 35 U.S.C. §112, first paragraph as being allegedly non-enabled. Applicants must respectfully disagree. The Examiner argues that "Applicant fails to set forth the criteria that defines 'a non-corneotoxic serine-threonine kinase inhibitor' Additionally applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. The

pharmaceutical art is unpredictable requiring each embodiment to be individually assessed for physiological activity" (Office Action, p. 2). Applicants must respectfully disagree.

It also appears that the Examiner has not considered the Applicants' arguments presented in the Preliminary Amendment filed with the present Continuation Application, nor did the Examiner consider the Declaration of one of the inventors, Dr. Paul Kaufman, which was concurrently filed with the Preliminary Amendment (should the Examiner need another copy of either of these documents, Applicants would be happy to fax them to the Office). In addition, in regards to the property of "non-corneotoxicity," Applicants provide a definition of this term in the Specification as filed (*See e.g.,* page 9, lines 8-17).

Applicants believe that they have fulfilled the requirements of 35 U.S.C. §112, first paragraph, and that the pending Claims 1-13 do not require undue experimentation on the part of the skilled artisan to ascertain the compounds that are encompassed by the Claims. As indicated in the Preliminary Amendment, "[t]he key word is 'undue' not 'experimentation.'" *In re Angstadt and Griffin*, 190 USPQ 214, 219 (CCPA 1976). "[A] considerable amount of experimentation is permissible . . . if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed . . . ." *Ex parte Jackson*, 217 USPQ 804, 807 (Bd. App. 1982); *In re Wands*, 8 USPQ 2d 1400, 1404 (CAFC 1988). The Examiner must not lose sight of the fact that experimentation is permissible, even considerable experimentation, "if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int'f. 1986).

For example, in order to determine if a particular serine threonine kinase inhibitor is encompassed by the present Claims, the compound must meet the functional definition of serine-threonine kinase inhibitors, not a structural definition. As more extensively described in the Preliminary Amendment, Applicants believe that more than sufficient guidance is provided in the Description of the Invention and the Examples to teach one of ordinary skill in the art to identify and use serine threonine kinase inhibitors that are useful in enhancing aqueous humor outflow. Applicants also believe that the factors set forth in *Ex parte Forman*

(*Ex parte Forman*, 230 USPQ 546 [1](Bd. Pat. App. & Int'f. 1986)) are met in the present Application. For example, Applicants strenuously contend that the application sets forth detailed protocols for screening any serine-threonine kinase inhibitor useful for enhancing aqueous humor outflow. This is reflected in the explicit definition of "serine-threonine kinase inhibitor" in the application (*See,* page 9, lines 1-7; and the detailed discussion of this class of compounds on page 26 line 25, through page 29, line 20). As indicated in the Preliminary Amendment, there are multiple Examples which teach how to evaluate serine-threonine kinase inhibitors (*See e.g.,* the summary of steps provided in Tables 2A and 2B).

Furthermore, the same screening procedures as those described in the Specification as filed, were utilized by Dr. Kaufman to identify other compounds with desirable activities (Kaufman Decl., ¶¶7-9). As stated in the Manual of Patenting Examination Procedures (MPEP), at 2164.04:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support . . . . As stated by the Court, 'it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain <u>why</u> it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." 439 F.2d at 224, 169 USPQ at 370. (emphasis in original).

As the Examiner has provided no evidence or explanation for doubting the truth or accuracy of any the statements in the present application, the Applicants' Specification must be presumed to fulfill the enablement requirement of 35 U.S.C. §112, first paragraph. Drs. Kaufman and Geiger's claims are specifically directed to kinase inhibitors that affect aqueous humor outflow (*e.g.,* H-7, ML-7, staurosporine, and KT-5926)(*See e.g.,* Kaufman Decl., ¶10).

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[1] The "Forman factors" used in making the determination of whether undue experimentation is necessary are set forth on page 547 of *Ex parte Forman*. These factors are: quantity of experimentation necessary; the amount of direction or guidance presented; the presence or absence of working examples; the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; and the breadth of the claims.

In specific, their work on H-7, ML-7, and staurosporine, shows that these compounds dramatically affect cell contractility and increase aqueous humor outflow facility via their junction and cytoskeleton-disrupting activities. Additional descriptions of these properties and characteristics are provided in the Specification as filed, as well as the Preliminary Amendment and Dr. Kaufman's Declaration.

The MPEP further states that "Applicant may submit factual affidavits under 37 CFR 1.132 or cite references to show what one skilled in the art knew at the time of filing the application. A declaration or affidavit is, itself, evidence that must be considered." (emphasis in original). As stated in the MPEP, the Examiner **must consider** the Declaration of Dr. Kaufman, and provide evidence as to why the Examiner doubts the truth or accuracy of any statement in the Specification. Applicants submit that although the Examiner has not met the burden of establishing non-enablement, Applicants through the Specification, as well as the supporting arguments contained within the Preliminary Amendment and Declaration of Dr. Paul Kaufman filed with the Preliminary Amendment, have more than met the enablement requirements of 35 U.S.C. §112, first paragraph. Applicants therefore respectfully request that this rejection be withdrawn.

2) Double-Patenting Rejection

The Examiner has provisionally rejected Claims 1-13 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent No. 5,798,380. In order to further their business interests and prosecution of the present application, but without acquiescing to the Examiner's arguments, Applicants are willing to file a terminal disclaimer to overcome any obviousness type double patenting rejection if Claims 1-13 are otherwise allowable.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicant's claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (415) 705-8410.

Respectfully submitted,
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